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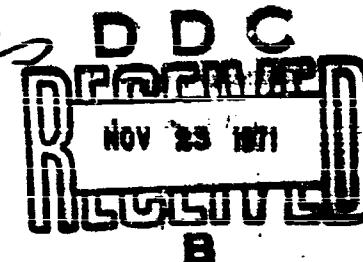
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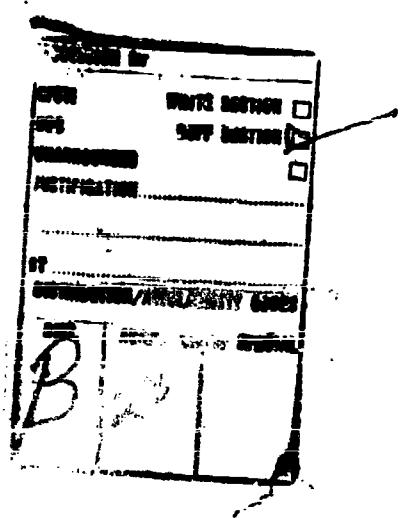
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## STUDY OF AN OUTBREAK OF VENEZUELAN ENCEPHALITIS IN VENEZUELA

[Article by Drs Armando Soto Escalona and Silvio A. Vaca, Department of Clinical Research, University of Zulia), and Dr Luis T. Finch (Venezuelan Health Service, Maracaibo); Investigacion Clinica, Spanish, Vol. 1, No. 1, 1968, pp. 45-57]

### Introduction

Venezuelan encephalitis has appeared in epidemic proportions in the Venezuelan portion of the Guajira, State of Zulia, since approximately July 1950 [5], and has existed in epidemic form for a period not longer than 10 years, although there are suspicions that it has been confused with other similar diseases [1]. By 1962 the virus had been isolated from patients in a severe epidemic which attacked the Guajira and extended to the eastern end of the country [1, 6]. In October 1968 the region experienced a new outbreak, which is analyzed in the present article.

### Description of the Epidemic

The affected region. The State of Zulia occupies the northwest part of Venezuela, between 71 and 73 degrees west longitude and 10 and 11 degrees north latitude. The Paez District lies in the northernmost part of the state and borders north and west on the Republic of Colombia, south on the District of the same state, and east on the Gulf of Venezuela. Its area is 3,140 square kilometers, and includes two municipalities: Chiquipa and Samanaica. In terms of vegetation three zones are distinguished in the district: a forest zone, a pre-desert zone, and a desert zone. The two latter regions were the ones most seriously affected by the epidemic; here the temperature is 29 degrees Centigrade in the shade with an annual rainfall less than 500 millimeters (Figure 1). The population estimate for 1968 was 28,000, with an average density of 8 inhabitants per square kilometer. In addition to the populated centers there are numerous widely spaced ranches.

Development of the epidemic. The situation was soon to be abnormal when a significant increase occurred in the number of febrile patients appearing at the Rural Medical Station in Paraguipoa, capital of the municipality of Guajira. An investigation performed around the village uncovered a large number

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of diseased horses and a certain number of dead horses. Previous epidemics helped in forming a provisional diagnosis of Venezuelan encephalitis, which was later confirmed by isolation of the virus from the blood of several patients.

Experience in Venezuelan encephalitis from the blood

Isolation and identification of the virus. The virus was isolated on serum from the acute phase of febrile patients, by inoculation of newborn Swiss white mice and in cultivated cells of the chick embryo [1]. Fourteen viruses were isolated from 14 inoculated mice. The identification was made in two of the mouse samples, using the following method of minor protection. The problem sample was divided in two, one part was mixed with serum which was immune to the virus of Venezuelan encephalitis (VEE) (immune horse serum, Lot 1, National Communicable Disease Center, Atlanta, Georgia); the other part was mixed with a phosphate buffer of pH of 7.4. Both mixtures were incubated at 37 degrees Centigrade for one hour and then inoculated intracerebrally into newborn Swiss white mice. The animals inoculated with the problem serum which had not been treated with anti-VEE serum died 20 hours after inoculation. The mice protected with immune serum were observed for one week and showed no signs of disease whatever.

Serological studies. Twenty pairs of serum, acute and convalescent, were studied using Clarke and Casals hemagglutination titration method [2] modified by Sever as a microtechnique [7] and employing kaolin to dilute the non-specific inhibitors. In 18 cases there was a clear increase in the titre of antibodies to the VEE virus (Table 1).

Criteria for classifying the evidence. Using the system employed in 1962 [1], four groups were considered. Group 1 included all those patients who showed three or more of the following symptoms: fever, chills, intense headaches, sclero-conjunctival congestion, facial palsy, conjunctivitis-erythema, cervical adenopathies, nausea, diarrhea, and vertigo. Group 2 was made up of patients with some of the foregoing symptoms and related focal manifestations such as nystagmus, meningeal symptoms, somnolence, convulsions, and delirium. Group 3 consisted of doubtful cases, very hard to distinguish from any other febrile condition. These patients were not included in the case studies. Group 4 contained all patients with clinically defined illnesses different from Venezuelan encephalitis.

Distribution throughout time. Figures 2 and 3 show the number of patients consulting the medical stations in Paraguáipos and Birmania daily beginning on 1 October 1968. A sudden increase can be observed beginning on 27 October and lasting until 1 November. The number of patients at the medical stations began to decline on the day control measures were begun. The epidemic curve for each municipality does not differ from the over-all curve for the entire district (Figure 4).

Rate of attack. Table II shows the population of the Ruiz District estimated as of 1 July 1968 and the rate of attack of the disease per 1,000 inhabitants. The villages most seriously affected were Paraguáipos, La Punta, Los Pilucos, Mariche, and El Cañito, located in a relatively small area shown

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in Figure 5. A total of 1,077 syndromes due to Venezuelan encephalitis were registered. Of these, 150 showed clear evidence of the nervous system. Only two deaths were attributable to the disease. All cases were in children under one year of age.

Table III shows the distribution of incidence of the disease in children. The highest incidence of the disease is observed in children under one year of age, a fact which can be seen more clearly in Table V. The difference in incidence in population groups above and below one year of age is statistically extremely significant. Among older people the incidence is much smaller. Table V shows the distribution of cases in children under one year of age, below one year and above 40, and in adults and in females. The other age groups show no significant difference.

The mortality rate is 1.4%. The highest mortality rate is in children under one year of age, a fact which can be seen in Table V. The mortality rates in the different age groups are as follows: 1.4% for children under one year of age, 0.7% for children between one and four years of age, 0.3% for children between four and 10 years of age, 0.2% for children between 10 and 19 years of age, 0.1% for children between 20 and 39 years of age, and 0.1% for adults. The difference is extremely significant and progressive with age. In the epidemic of 1962 there was no difference in mortality rates based on sex.

### Discussion

The disease has been known in epizootic form in the Guajira since 1936 [4], although Gallo and Vegelvang [5] called it Venezuelan encephalitis in 1930. Encephalitis among humans, however, was not described until 1959, possibly because of confusion with other febrile diseases. According to observations by Avilán [1] the malaria epidemics in the region in 1910, 1915, 1916, 1920, 1926-27, 1931, 1933, 1935, 1940, 1945, 1950, 1954, 1958, and 1962 were all due to epidemics of Venezuelan encephalitis. More recently, in 1962, outbreaks diagnosed as influenza could also be due to Venezuelan encephalitis when it is noted that there were also cases of encephalitis in the burros [1]. It was not until 1962 that the presence of the Venezuelan encephalitis virus was confirmed in patients during an epidemic which occurred in the region [6].

The fact that the mortality rate is 1.4% in children under 6 years of age indicates that the virus has not been eliminated from the population since the epidemic of 1962. This agrees with Rymer's observations (to be published) on the absence of antibodies against Venezuelan encephalitis among children under 5 years of age in the Guajira in 1967. Considering the probable history of the disease in the area, it can be concluded that the disease has a cyclic activity and that there are no cases of the disease in the region between epidemics.

Some authors [3, 6] have reported that there is a progressive disappearance of a certain type of antibodies in individuals who have suffered Venezuelan encephalitis. But the epidemiological data do not support this apparent loss does not modify the acquired resistance to the disease. It is observed that mortality rates are progressively lower among the older ages, and this, in a population uniformly exposed to the causative agent, is a demonstration of immunity. Furthermore, one can observe a first-time infection in children under one year old, which can be explained by the presence of transmitted maternal antibodies. It can be concluded from the foregoing that the disease confers long-lasting immunity.

In addition to the 1,077 cases examined clinically, there were around 500 consulting patients with febrile conditions which were not diagnosed as Venezuelan encephalitis because they did not meet the established criteria but

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who probably had very benign cases of the disease. According to Ryder (in publication) it is also probable that there were many subclinical infections caused by this virus, since high titers of antibodies to the virus were found in zones where no epidemics of Venezuelan encephalitis had been described, such as the region to the south of Lake Maracaibo. The mortality rate of the disease must have been much greater than the epidemic.

The serious neurological cases represented 1.1% of the total of patients, a high percentage in comparison to the 0.1% mortality rate which the 1961 was calculated at 6%. If we include among our cases all those consulting patients placed above in group 3, we arrive at 1.5% of serious neurological cases, a number which is in any case higher than the 0.1% mortality. The number of deaths attributable to the disease was 0.1%, or 1.0% mortality, much lower than the figure for the previous epidemic [3].

No logical explanation was found for the sex difference for females among children less than one year old and males among those over 40. It should be noted that the difference was observed only in the 1961 epidemic.

#### Summary

An epidemic of Venezuelan encephalitis, the first in the region, began in October 1968 in the District of Paez, State of Zulia, and continued until May 1969. A total of 1,077 cases of the disease were registered, 100 of which exhibited evident attack on the nervous system. Two deaths were attributed to the encephalitis, both in children less than one year old. There was a small number of cases among children less than 6 years old; this is in agreement with the last encephalitis epidemic in the region, which points to the low virulence of the virus. It was concluded that the virus is inactive in the inter-epidemic periods. The immunity conferred by the virus is apparently short lived, which, as indicated by the small number of older patients and children less than one year old, the latter protected by transmitted maternal antibodies.

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### Section 1 Test 5



Figura N° 1. Mapa del Distrito Pisco en el cual se indican los parques y canteras abiertas por el hombre.

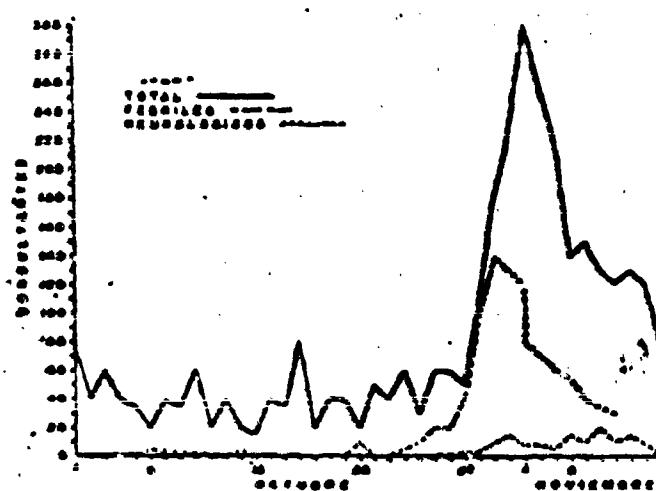


Figura N° 2. Número de consultantes a la Medicina Rural de Paraguaimpu desde el 1º de Octubre de 1962, en número de apacuadas del bosque al 23 del mismo año.

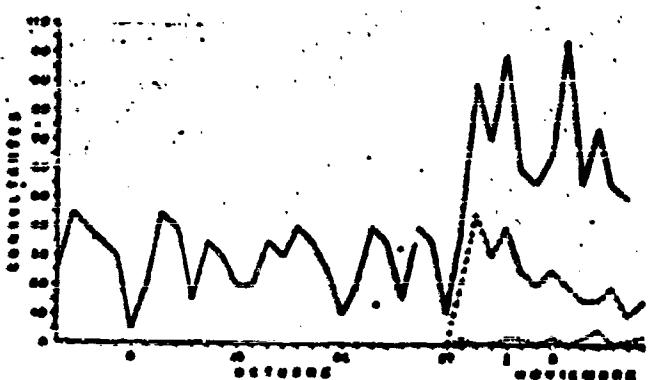


Figura 20-2. Número de consultas de la Medicina Rural de Guatemala durante el año 1950 de acuerdo a número de consultas. Aunque se observa un aumento considerable de las consultas individuales y consultas, la cifra es cada vez mayor y de menor cantidad. (Fuente: *Avances en la medicina rural en Guatemala*, 1950).

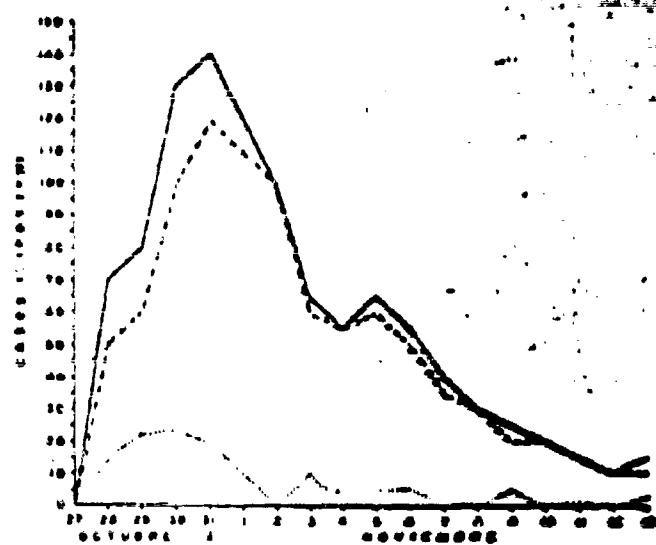


Figura N° 4. Curva epidémica para todo el Distrito y para ambos Municipios. La epidémica se produce principalmente a espaldas del Municipio Guatire. El Municipio Almendral continúa poco a la derecha de la curva. (Parquejunto 1944; Planos 1944; Distrito 1944-1945).

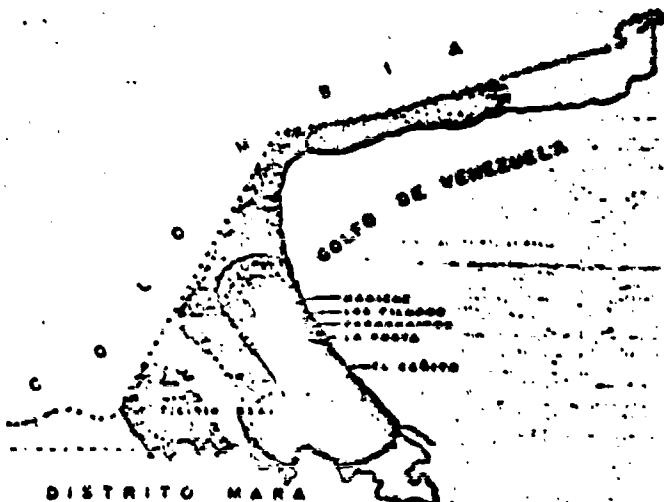


Figura N° 8. Mapa del Distrito en el cual se indican las zonas asumimiento asentadas. En la base en negro se registraron más de 600 casas. Los asentamientos ubicados en la zona gris aparecieron entre 200 y 300 casas. El resto de los 1.077 casas se concentraron en la zona sin sombrear.

#### FIGURE CAPTIONS

Figure 1. Map of the District of Peix, indicating villages and settlements affected by the outbreak.

Figure 2. Number of consultants at the Health Station of Paraguipoa beginning on 1 October 1968. The beginning of the outbreak on 27 October is visible.

Figure 3. Number of consultants at the Health Station of Sinaúmica during the same period. Although a slight increase in the number of febrile and convulsive cases can be seen, the curve is much flatter and lower. (Febrile: -----, neurological -----, total: - - - - -)

Figure 4. Epidemic curve for the period 1 October to 1 November for both municipalities. The epidemic affected primarily the Municipality of Paraguipoa. The Municipality of Sinaúmica contributed little to the total number of cases on the curve. (Paraguipoa -----, Sinaúmica -----, Peix District - - - - -)

Figure 5. Map of the District, showing the two heavily affected regions. The region in black registered more than 300 cases. The villages in the gray region reported between 200 and 300 cases. A total of 1,077 cases were found in the checked region.

#### Spanish Words Used in Figures

total	total
febril	febrile
neurologicos	neurological
consultantes	consultants
Octubre	October
Noviembre	November
Casos	cases
Tipos I y III	Types I and III

TABLAS 1 THRU 5

TABLA I

1 TITULOS DE ANTICUERPOS INHIBIDORES DE LA HEMAGLUTINACION CONTRA EL VIRUS EEV EN 20 PACIENTES.

2 NOMBRE	3 EDAD	4 SUERO AGUDO	5 SUERO CONVALESCIENTE
L.G.	19	<10	80
N.M.	50	<10	>1280
N. CR.	14	<10	320
E.G.	30	<10	160
E.G.	38	<10	160
J.A.	26	<10	<10
A.V.	26	<10	160
R.P.	10	<10	160
V.M.	6	<10	160
A.P.	24	<10	320
N.C.	17	<10	160
M.G.	29	<10	>1280
J.R.	11	<10	320
I.G.	10	<10	320
P.F.	20	<10	>1280
J.G.	25	<10	320
C.C.	13	<10	320
M.M.	38	<10	<10
V.G.	5	80	320
B.B.	-	40	320

TABLA II

2 ENCEFALITIS EQUINA VENEZOLANA. DISTRITO PAEZ, ESTADO ZULIA. 1968. RELACION DE CASOS POR MUNICIPIOS. TASAS DE ATAQUE POR 1.000 HABITANTES

2 MUNICIPIO	3 POBLACION ESTIMADA	4 NUMERO DE CASOS	5 CASOS POR 1.000
Guajira	13,937	957	68,7
Sinamaica	4,459	120	26,9
Distrito Paez	18,396	1,077	58,4

6 Para el 1<sup>o</sup> de julio de 1968.

TABLA III

TABLA IV

2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
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TABLES

Table I

1. Titres of antibodies inhibiting hemagglutination against the VEE virus in 20 patients
2. Name
3. Age
4. Acute serum
5. Convalescent serum

Table II

1. Venezuelan equine encephalitis, Paez District, State of Zulia, 1968. Numbers of cases by municipalities and rates of attack per 1,000 inhabitants
2. Municipality
3. Estimated population
4. Number of cases
5. Cases per 1,000 inhabitants
6. As of 1 July 1968

Table III

1. Distribution of cases by age groups. Rates of attack per 1,000 inhabitants
2. Age groups
3. Guajira Municipality
4. Sinamaica Municipality
5. Paez District
6. Cases
7. Estimated population
8. Rate
9. Up to one year old
10. One to 6 years old
11. Forty and older
12. Age unknown
13. Total

Table IV

1. Differences in mortality rates between those above and below 6 years of age
2. Age groups
3. Guajira Municipality
4. Sinamaica Municipality
5. Paez District
6. Cases
7. Estimated population
8. Rate
9. Less than 6 years old
10. Over 6 years old

Table V

1. Distribution of cases by age groups and by the rate of attack per 1,000 inhabitants
2. Age groups
3. Guajira Municipality
4. Sinanica Municipality
5. Pez District
6. Cases
7. Estimated population
8. Rate
9. Up to one year old
10. One to 6 years old
11. Forty and older
12. Age unknown
13. Total

V Male  
M Female

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